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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/895,263	07/02/2001	Wei Wu He	PF140C2	3220

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EXAMINER
HUYNH, PHUONG N

ART UNIT	PAPER NUMBER
1644	10

DATE MAILED: 06/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/895,263	HE ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on th cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 March 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☒ Claim(s) *31-39, 42-52, 54-72, 75-86, and 88-107* is/are pending in the application.

4a) Of the above claim(s) *51,52 and 84-86* is/are withdrawn from consideration.

5)☒ Claim(s) *98-107* is/are allowed.

6)☒ Claim(s) *31, 34-35, 38-39, 42-50, 53, 55-57, 59-83 and 87-97* is/are rejected.

7)☒ Claim(s) *32,33,36,37,54 and 58* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Claims 31-39, 42-52, 54-72, 75-86, and 88-107 are pending.

2. The request to rejoin the method claims if the elected product claims are found allowable in In re Ochiai and In re Brouwer is acknowledged.

3. In view of the amendment filed 3/7/03, the following objection and rejections remain.

4. The disclosure stands objected to because of the following informalities: the abstract and the title of instant application does not reflect on the subject being claimed, which is the antibodies to the ICE-LAP3 and ICE-LAP4. Appropriate action is required.

5. The references on PTO 1449, filed 10/28/02, have been fully considered.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 31, 34-35, 38-39, 42-50, 53, 55-57, 59-83 and 87-97 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for (1) an isolated antibody or fragment thereof that specifically binds to a protein selected from the group consisting of (a) a protein consisting of amino acid residues 1 to 303 of SEQ ID NO: 2; (b) a protein consisting of amino acid residues 2 to 303 of SEQ ID NO: 2; (e) a protein consisting of amino acid residues 1 to 277 of SEQ ID NO: 4; (f) a protein consisting of amino acid residues 2 to 277 of SEQ ID NO: 4, (2) the said antibody or antibody fragment thereof that specifically binds to protein (a), (b), (e) or (f), (3) the said antibody or fragment thereof which is a human antibody, a polyclonal antibody, a monoclonal antibody, a chimeric antibody, a humanized antibody, a single chain antibody and an Fab fragment, (4) An labeled antibody or fragment thereof of that specifically binds to a protein selected from the group consisting of (a) a protein consisting of amino acid residues 1 to 303 of SEQ ID NO: 2; (b) a protein consisting of amino acid residues 2 to 303 of SEQ ID NO: 2; (e) a protein consisting of amino acid residues 1 to 277 of SEQ ID NO: 4; (f) a protein consisting of amino acid residues 2 to 277 of SEQ ID NO: 4 wherein the antibody or

fragment thereof is labeled, (5) the labeled antibody or fragment thereof wherein the label is an enzyme, (6) the said antibody or antibody fragment thereof wherein said antibody or fragment thereof specifically binds to said protein in an ELISA, (7) A hybridoma that produces the antibody that specifically binds to a protein selected from the group consisting of (a) a protein consisting of amino acid residues 1 to 303 of SEQ ID NO: 2; (b) a protein consisting of amino acid residues 2 to 303 of SEQ ID NO: 2; (e) a protein consisting of amino acid residues 1 to 277 of SEQ ID NO: 4; (f) a protein consisting of amino acid residues 2 to 277 of SEQ ID NO: 4, (8) an isolated antibody or fragment thereof obtained from an animal that has been immunized with a protein comprising the amino acid sequence of amino acid residues 1 to 303 of SEQ ID NO: 2; a protein comprising the amino acid sequence of amino acid residues 1 to 277 of SEQ ID NO: 4, (9) the antibody or fragment thereof obtained from an animal that has been immunized with a protein comprising the amino acid sequence of amino acid residues 1 to 303 of SEQ ID NO: 2; a protein comprising the amino acid sequence of amino acid residues 1 to 277 of SEQ ID NO: 4 which is a monoclonal antibody, a chimeric antibody, a polyclonal antibody, a humanized antibody, a single chain antibody and an Fab fragment, (10) An isolated antibody or fragment thereof that specifically binds to a protein selected from the group consisting of: (a) a protein consisting of the full-length polypeptide encoded by the cDNA contained in ATCC Deposit Number 75875 or 75873, (b) a protein consisting of the mature form of the polypeptide encoded by the cDNA contained in ATCC Deposit Number 75875 or 75873, (11) the said antibody or fragment thereof that specifically binds to a protein selected from the group consisting of: (a) a protein consisting of the full-length polypeptide encoded by the cDNA contained in ATCC Deposit Number 75875 or 75873, (b) a protein consisting of the mature form of the polypeptide encoded by the cDNA contained in ATCC Deposit Number 75875 or 75873 is a human antibody, a polyclonal antibody, a monoclonal antibody, a chimeric antibody, a humanized antibody, a single chain antibody, and an Fab fragment, (12) the labeled antibody or fragment thereof of that specifically binds to a protein selected from the group consisting of: (a) a protein consisting of the full-length polypeptide encoded by the cDNA contained in ATCC Deposit Number 75875 or 75873, (b) a protein consisting of the mature form of the polypeptide encoded by the cDNA contained in ATCC Deposit Number 75875 or 75873 wherein the antibody or fragment is labeled, (13) the said labeled antibody wherein the label is an enzyme, (14) the said antibody or fragment thereof wherein said antibody or antibody fragment binds to said protein in an ELISA, (15) a hybridoma that produces the antibody of that specifically binds to a protein selected from the

group consisting of: (a) a protein consisting of the full-length polypeptide encoded by the cDNA contained in ATCC Deposit Number 75875 or 75873, (b) a protein consisting of the mature form of the polypeptide encoded by the cDNA contained in ATCC Deposit Number 75875 or 75873, (16) an isolated antibody or fragment thereof obtained from an animal that has been immunized with a protein selected from the group consisting of: (a) a protein comprising the amino acid a protein consisting of the full-length polypeptide encoded by the cDNA contained in ATCC Deposit Number 75875 or 75873, (b) a protein consisting of the mature form of the polypeptide encoded by the cDNA contained in ATCC Deposit Number 75875 or 75873, (c) a protein comprising an amino acid sequence consisting of at least 30 contiguous amino acid residues of the polypeptide encoded by the cDNA contained in ATCC Deposit Number 75875 or 75873, (d) a protein comprising an amino acid sequence consisting of at least 50 contiguous amino acid residues of the polypeptide encoded by the cDNA contained in ATCC Deposit Number 75875 or 75873 wherein said antibody or fragment thereof specifically binds to said amino acid sequence, (17) the said antibody or fragment thereof obtained from an animal immunized with said protein mentioned above is a monoclonal, chimeric, polyclonal, humanized, single chain antibody and an Fab fragment, (18) An isolated antibody or fragment thereof that specifically binds an ICE-LAP3 protein purified from a cell culture wherein said ICE-LAP3 protein is encoded by a polynucleotide encoding amino acids 1 to 303 of SEQ ID NO:2 operatively associated with a regulatory sequence that controls the expression of said polynucleotide, the isolated antibody or fragment thereof that specifically binds an ICE-LAP3 protein purified from a cell culture wherein said ICE-LAP3 protein is encoded by a polynucleotide encoding amino acids 1 to 303 of SEQ ID NO:2 operatively associated with a regulatory sequence that controls the expression of said polynucleotide is a monoclonal antibody, a human antibody, a chimeric antibody, a polyclonal antibody, a humanized antibody, a single chain antibody and an Fab fragment, (19) the said antibody or fragment thereof wherein said antibody or fragment thereof specifically binds to said protein in an ELISA, (20) An isolated antibody or fragment thereof that specifically binds an ICE-LAP4 protein purified from a cell culture wherein said ICE-LAP4 protein is encoded by a polynucleotide encoding amino acids 1 to 277 of SEQ ID NO: 4 operatively associated with a regulatory sequence that controls the expression of said polynucleotide, the isolated antibody or fragment thereof that specifically binds an ICE-LAP3 protein purified from a cell culture wherein said ICE-LAP3 protein is encoded by a polynucleotide encoding amino acids 1 to 277 of SEQ ID NO: 4 operatively associated with a regulatory sequence that controls the expression of said

polynucleotide is a monoclonal antibody, a human antibody, a chimeric antibody, a polyclonal antibody, a humanized antibody, a single chain antibody and an Fab fragment, (21) the said antibody or fragment thereof wherein said antibody or fragment thereof specifically binds to said protein in an ELISA for sandwich assays (page 17) or detection assays (page 18), **does not** reasonably provide enablement for (1) *any* isolated antibody or fragment thereof that specifically binds to *any* protein consisting of *any* portion of SEQ ID NO: 2, wherein said portion "**comprises**" at least 30 or 50 contiguous amino acid residues of SEQ ID NO: 2 or 4, (2) the isolated antibody or fragment thereof that specifically binds to a protein selected from the group consisting of *any* protein consisting of a portion of SEQ ID NO: 2, wherein said portion "**comprises**" at least 30 or 50 contiguous amino acid residues of SEQ ID NO: 2 or 4 wherein the antibody is a human antibody, a polyclonal antibody, a monoclonal antibody, a chimeric antibody, a humanized antibody, a single chain antibody, and an Fab fragment, (3) *any* antibody or fragment thereof of *any* isolated antibody or fragment thereof that specifically binds to a protein selected from the group consisting of a protein consisting of a portion of SEQ ID NO: 2, wherein said portion "**comprises**" at least 30 or 50 contiguous amino acid residues of SEQ ID NO: 2 or 4 is labeled, (4) the said labeled antibody or fragment thereof wherein the label is an enzyme, (5) *any* isolated cell or hybridoma that produces "**antibody fragment thereof**" of *any* isolated antibody or fragment thereof that specifically binds to a protein such as the ones recited in claims 31 (a) through (h), (6) a method of detecting an ICE0LAP 3 or 4 protein in a biological sample using any antibody mentioned above, (7) *any* isolated antibody or fragment thereof obtained from an animal that has been immunized with a protein "**comprising**" the amino acid sequence of amino acid of SEQ ID NO: 2 **consisting** of at least 30 or 50 contiguous amino acid residues of SEQ ID NO: 2, (8) *any* isolated antibody or fragment thereof obtained from an animal that has been immunized with a protein "**comprising**" the amino acid sequence of amino acid of SEQ ID NO: 4 "**consisting**" of at least 30 or 50 contiguous amino acid residues of SEQ ID NO: 4, (9) the antibody or fragment thereof obtained from an animal immunized with a protein selected from the group consisting of a protein "**comprising**" the amino acid sequence of amino acid of SEQ ID NO: 2 consisting of at least 30 or 50 contiguous amino acid residues of SEQ ID NO: 2, (10) the antibody or fragment thereof obtained from an animal immunized with a protein selected from the group consisting of a protein "**comprising**" the amino acid sequence of amino acid of SEQ ID NO: 4 consisting of at least 30 or 50 contiguous amino acid residues of SEQ ID NO: 4, (11) The said antibodies is a chimeric antibody, a polyclonal antibody, a humanized

antibody, a single chain antibody and an Fab fragment, (12) *any* isolated antibody or fragment thereof that specifically binds to *any* protein consisting of *any* "portion" of the polypeptide encode by the cDNA contained in ATCC Deposit Number 75875 or 75873, wherein said portion "**comprises**" at least 30 or 50 contiguous amino acid residues of the polypeptide encoded by the cDNA contained in ATCC Deposit Number 75875 or 75873, (13) the antibody or fragment thereof that specifically binds to *any* protein consisting of a portion of the polypeptide encode by the cDNA contained in ATCC Deposit Number 75875 or 75873, wherein said portion "**comprises**" at least 30 or 50 contiguous amino acid residues of the polypeptide encoded by the cDNA contained in ATCC Deposit Number 75875 or 75873 that specifically binds to protein such as the ones recited in claims 65-74, (14) the antibody or fragment thereof that specifically binds to *any* protein consisting of a portion of the polypeptide encode by the cDNA contained in ATCC Deposit Number 75875 or 75873, wherein said portion "**comprises**" at least 30 or 50 contiguous amino acid residues of the polypeptide encoded by the cDNA contained in ATCC. Deposit Number 75875 or 75873 is a human antibody, a polyclonal antibody, a monoclonal antibody, a chimeric antibody, a humanized antibody, a single chain antibody, and an Fab fragment, (15) *any* isolated antibody or fragment thereof mentioned above which is labeled, (16) *any* antibody or fragment thereof mentioned above which is labeled wherein the label is an enzyme, (17) *any* antibody or fragment thereof mentioned above wherein said antibody or fragment specifically binds to said protein in an ELISA, (18) *any* isolated cell or hybridoma that produces "**fragment thereof**" of antibody that specifically binds to any protein consisting of a portion of the polypeptide encode by the cDNA contained in ATCC Deposit Number 75875 or 75873, wherein said portion "**comprises**" at least 30 or 50 contiguous amino acid residues of the polypeptide encoded by the cDNA contained in ATCC Deposit Number 75875 or 75873, and (19) an isolated antibody or fragment thereof obtained from an animal that has been immunized with *any* protein mentioned above for sandwich assays (page 17) or detection assays (page 18). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working

examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only two polypeptides of interleukin-1 beta converting enzyme like apoptosis protease 3 (ICE-LAP3) of SEQ ID NO: 2 and ICE-LAP4 of SEQ ID NO: 4 encoded by cDNAs contained in ATCC Deposit Number 75875, and 75873, respectively. The specification further discloses antibodies such as polyclonal, monoclonal, chimeric, single chain, and humanized antibodies as well as antibody fragment thereof such as Fab fragments that binds specifically to polypeptides of interleukin-1 beta converting enzyme like apoptosis protease 3 (ICE-LAP3) of SEQ ID NO: 2 and ICE-LAP4 of SEQ ID NO: 4 encoded by cDNAs contained in ATCC Deposit Number 75875, and 75873, respectively for detection assays such as sandwich assays (page 17) or detection assays (page 18).

The specification does not provide *any* guidance as how to make and use *any* isolated antibody or fragment thereof that binds to *any* protein consisting of *any* portion of SEQ ID NO: 2 or 4 wherein said portion "comprises" at least any 30 or 50 contiguous amino acid residues of SEQ ID NO: 2 or 4 because the term "comprising" is open-ended. It expands the portion to include additional amino acids at either or both end of said portion. There is insufficient guidance as to what are the undisclosed amino acids to be added. There is no showing of the binding specificity of the claimed antibody that could bind to protein consisting of a portion of SEQ ID NO: 2 wherein the portion has extra undisclosed amino acids in addition to any 30 or 50 contiguous amino acid residues of SEQ ID NO: 2 or 4. There is insufficient guidance as to binding specificity of the claimed antibody or fragment thereof obtained from an animal that has been immunized with *any* protein consisting of any portion of SEQ ID NO: 2 or 4 wherein said portion "comprises" at least any 30 or 50 contiguous amino acid residues of SEQ ID NO: 2 or 4 because of the following reasons. First, there is insufficient guidance as to which portion such as which 30 or 50 amino acids of SEQ ID NO: 2 or 4 to be used for generating any antibody that would bind specifically to SEQ ID NO: 2 or 4. Second, the term "comprising" is open-ended. It expands the undisclosed portion of SEQ ID NO: 2 or 4 to include additional amino acids at either or both ends of said portion. Third, there is no showing that immunizing an animal with any undisclosed protein would generate antibody such as monoclonal, polyclonal, chimeric, humanized, single chain and antigen binding fragment thereof that would bind specifically to

SEQ ID NO: 2 or 4. Four, there are no working examples of any antibody mentioned above ever been made, much less about the binding specificity of the antibodies being claimed. Five, there is no guidance as to the specific amino acid residues that makes up the antigenic determinant for which the antibody binds.

Ngo *et al* teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure/function will require guidance (See Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). Given the lack of guidance and working examples, predicting what changes can be made to the amino acid sequence mentioned above that after insertion and/or modification will retain both structure and have similar function as SEQ ID NO: 2, SEQ ID NO: 4, or the polypeptide encoded by the cDNAs contained in ATCC Deposit Number 75875, or 75873 is unpredictable. Furthermore, it is well known in the art at the time the invention was made that antibody epitopes (B cell epitopes) are not linear and are comprised of complex three-dimensional array of scattered residues which will fold into specific conformation that contribute to binding (See Kuby 1994, page 94, in particular).

Kuby *et al* teach that immunizing a peptide versus a full-length polypeptide may result in **antibody specificity** that differs from antibody specificity directed against the native full-length polypeptide. Without the specific amino acid residues, it is unpredictable which undisclosed antibody generated from an indefinite number of undisclosed polypeptide will have the same antibody binding specificity as an antibody generated from the full length polypeptide or protein of SEQ ID NO: 2, or SEQ ID NO: 4 or the polypeptide encoded by the cDNAs contained in ATCC Deposit Number 75875, or 75873, in turn, would be useful for any purpose.

As to claim 53 (c), (d), (g) (h), 87 (c), (d), (g) (h), although the claim has been amended, it is not clear if the claimed antibody or fragment thereof obtained from an animal that has been immunized with a protein comprising an amino acid sequence of SEQ ID NO: 2, SEQ ID NO: 4, the polypeptide encoded by the cDNA contained in the ATCC Deposit Number 75875 or 75873, or a protein consisting of at least 30 or 50 contiguous amino acid residues of SEQ ID NO: 2, SEQ ID NO: 4, the polypeptide encoded by the cDNA contained in the ATCC Deposit Number 75875 or 75873 as written. Given the ambiguity of the protein used to immunize the animal, any antibody obtained from any animal using any undisclosed protein is not enabled.

As to claims 42-48, 62-63, and 75-81, since the antibody mentioned above is not enable, it follows that any monoclonal antibody, any chimeric antibody, any polyclonal antibody and humanized antibody and labeled antibody obtained from *any* animal that has been immunized with said undisclosed protein mentioned above are not enable. It also follows that the method of using the undisclosed antibody is not enabled.

With regard to any isolated cell or hybridoma (claims 49-50, and 82-83) that produce "antibody fragment thereof", it is well known that cell line and hybridoma produce the whole antibody and not the antibody fragment.

Harlow *et al* teach a method of producing antibody fragment wherein the fragment is Fab or F(ab')2 fragment by enzymatic cleavage using enzyme such as pepsin or papain (See pages 626-629, in particular).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the lack of working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

Applicants' arguments filed 3/7/03 have been fully considered but are not found persuasive.

Applicants' position is that (1) even thought the claim uses the word "comprises" to specify the portion of SEQ ID NO: 2, the recited protein nevertheless consists of a portion of SEQ ID NO: 2. (2) Applicants have amended claims 53 and 87 to specify with even greater clarity that the recited amino acid sequences to which the antibody specifically binds are derived from SEQ ID NO: 2, SEQ ID NO: 4 or the deposited cDNAs. (3) Claims 49-50 and 82-83 are directed to an isolated cell or a hybridoma that produces an antibody or fragment of an antibody. Whether a cell produces the whole antibody or a fragment of the antibody is merely a question of which coding sequences the cell is engineered with. Hybridoma can also produce either an entire antibody or a fragment of an antibody, see Exhibit A. Ochi et al reference points out that a hybridoma cell line can give rise to subclones which lack various portions of an immunoglobulin molecule.

However, there is insufficient guidance as to which portion of SEQ ID NO: 2, SEQ ID NO: 4 or the polypeptides encoded by the deposited cDNA that the claimed antibody is supposed to bind (binding specificity). Further, the term comprising is opened-ended. The specification

does not provide *any* guidance as how to make and use *any* isolated antibody or fragment thereof that binds to *any* protein consisting of any portion of SEQ ID NO: 2 or 4 wherein said portion "comprises" at least any 30 or 50 contiguous amino acid residues of SEQ ID NO: 2 or 4 because the term "comprising" is open-ended. It expands the portion to include additional amino acids at either or both end of said portion. There is insufficient guidance as to what are the undisclosed amino acids to be added. There is no showing that the claimed antibody could bind to protein consisting of a portion of SEQ ID NO: 2 wherein the portion has extra undisclosed amino acids in addition to any 30 or 50 contiguous amino acid residues of SEQ ID NO: 2 or 4. There is insufficient guidance as to the binding specificity of the claimed antibody or fragment thereof obtained from an animal that has been immunized with *any* protein consisting of any portion of SEQ ID NO: 2 or 4 wherein said portion "comprises" at least any 30 or 50 contiguous amino acid residues of SEQ ID NO: 2 or 4 because of the following reasons.

First, there is insufficient guidance as to which portion such as which 30 or 50 amino acids of SEQ ID NO: 2 or 4 to be used for generating any antibody that would bind specifically to SEQ ID NO: 2 or 4. Second, the term "comprising" is open-ended. It expands the undisclosed portion of SEQ ID NO: 2 or 4 to include additional amino acids at either or both ends of said portion. Third, there is no showing that immunizing an animal with any undisclosed protein would generate antibody such as monoclonal, polyclonal, chimeric, humanized, single chain and antigen binding fragment thereof that would bind specifically to SEQ ID NO: 2 or 4. Four, there are no working examples of any antibody mentioned above ever been made, much less about the binding specificity of the antibodies being claimed. Five, there is no guidance as to the specific amino acid residues that makes up the antigenic determinant for which the antibody binds.

Ngo *et al* teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure/function will require guidance (See Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). Given the lack of guidance and working examples, predicting what changes can be made to the amino acid sequence mentioned above that after insertion and/or modification will retain both structure and have similar function as SEQ ID NO: 2, SEQ ID NO: 4, or the polypeptide encoded by the cDNAs contained in ATCC Deposit Number 75875, or 75873 is unpredictable. Furthermore, it is well known in the art at the time the invention was made that antibody epitopes (B cell epitopes) are not linear and are comprised of complex three-dimensional array of scattered residues which

will fold into specific conformation that contribute to binding (See Kuby 1994, page 94, in particular).

Kuby *et al* teach that immunizing a peptide versus a full-length polypeptide may result in **antibody specificity** that differs from antibody specificity directed against the native full-length polypeptide. Without the specific amino acid residues, it is unpredictable which undisclosed antibody generated from an indefinite number of undisclosed polypeptide will have the same antibody binding specificity as an antibody generated from the full length polypeptide or protein of SEQ ID NO: 2, or SEQ ID NO: 4 or the polypeptide encoded by the cDNAs contained in ATCC Deposit Number 75875, or 75873, in turn, would be useful for any purpose.

As to claim 53 (c), (d), (g) (h), 87 (c), (d), (g) (h), although the claim has been amended, it is not clear if the claimed antibody or fragment thereof obtained from an animal that has been immunized with a protein comprising an amino acid sequence of SEQ ID NO: 2, SEQ ID NO: 4, the polypeptide encoded by the cDNA contained in the ATCC Deposit Number 75875 or 75873, or a protein consisting of at least 30 or 50 contiguous amino acid residues of SEQ ID NO: 2, SEQ ID NO: 4, the polypeptide encoded by the cDNA contained in the ATCC Deposit Number 75875 or 75873 as written. Given the ambiguity of the protein used to immunize the animal, any antibody obtained from any animal using any undisclosed protein is not enabled.

As to claims 42-48, 62-63, and 75-81, since the antibody mentioned above is not enable, it follows that any monoclonal antibody, any chimeric antibody, any polyclonal antibody and humanized antibody and labeled antibody obtained from *any* animal that has been immunized with said undisclosed protein mentioned above are not enable. It also follows that the method of using the undisclosed antibody is not enabled.

In response to Applicant's argument in item 3, the Ochi et al reference is irrelevant to the claimed hybridoma that produces the antibody fragment that specifically binds to protein as set forth in claims 31 and 64. There is no guidance as to which coding sequences the cell or hybridoma is engineered with to produce the antibody fragment that specifically binds to protein as set forth in claims 31 and 64. There is no working example demonstrating that the claimed hybridoma cell line give rise to subclones which lack various portion of an immunoglobulin molecule and the antibody produced from that particular subclone still binds to any protein as set forth in claims 31 and 64.

8. Claims 31, 34-35, 38-39, 42-50, 53, 55-57, 59-83 and 87-97 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of (1) *any* isolated antibody or fragment thereof that specifically binds to *any* protein consisting of *any* portion of SEQ ID NO: 2, wherein said portion "**comprises**" at least 30 or 50 contiguous amino acid residues of SEQ ID NO: 2 or 4, (2) the isolated antibody or fragment thereof that specifically binds to a protein selected from the group consisting of *any* protein consisting of a portion of SEQ ID NO: 2, wherein said portion "**comprises**" at least 30 or 50 contiguous amino acid residues of SEQ ID NO: 2 or 4 wherein the antibody is a human antibody, a polyclonal antibody, a monoclonal antibody, a chimeric antibody, a humanized antibody, a single chain antibody, and an Fab fragment, (3) *any* antibody or fragment thereof of *any* isolated antibody or fragment thereof that specifically binds to a protein selected from the group consisting of a protein consisting of a portion of SEQ ID NO: 2, wherein said portion "**comprises**" at least 30 or 50 contiguous amino acid residues of SEQ ID NO: 2 or 4 is labeled, (4) the said labeled antibody or fragment thereof wherein the label is an enzyme, (5) *any* isolated cell or hybridoma that produces "**antibody fragment thereof**" of *any* isolated antibody or fragment thereof that specifically binds to a protein such as the ones recited in claims 31 (a) through (h), (6) a method of detecting an ICE0LAP 3 or 4 protein in a biological sample using any antibody mentioned above, (7) *any* isolated antibody or fragment thereof obtained from an animal that has been immunized with a protein "**comprising**" the amino acid sequence of amino acid of SEQ ID NO: 2 **consisting** of at least 30 or 50 contiguous amino acid residues of SEQ ID NO: 2, (8) *any* isolated antibody or fragment thereof obtained from an animal that has been immunized with a protein "**comprising**" the amino acid sequence of amino acid of SEQ ID NO: 4 "**consisting**" of at least 30 or 50 contiguous amino acid residues of SEQ ID NO: 4, (9) the antibody or fragment thereof obtained from an animal immunized with a protein selected from the group consisting of a protein "**comprising**" the amino acid sequence of amino acid of SEQ ID NO: 2 consisting of at least 30 or 50 contiguous amino acid residues of SEQ ID NO: 2, (10) the antibody or fragment thereof obtained from an animal immunized with a protein selected from the group consisting of a protein "**comprising**" the amino acid sequence of amino acid of SEQ ID NO: 4 consisting of at least 30 or 50 contiguous amino acid residues of SEQ ID NO: 4, (11) The said antibodies is a chimeric

antibody, a polyclonal antibody, a humanized antibody, a single chain antibody and an Fab fragment, (12) *any* isolated antibody or fragment thereof that specifically binds to *any* protein consisting of *any* "portion" of the polypeptide encode by the cDNA contained in ATCC Deposit Number 75875 or 75873, wherein said portion "**comprises**" at least 30 or 50 contiguous amino acid residues of the polypeptide encoded by the cDNA contained in ATCC Deposit Number 75875 or 75873, (13) the antibody or fragment thereof that specifically binds to *any* protein consisting of a portion of the polypeptide encode by the cDNA contained in ATCC Deposit Number 75875 or 75873, wherein said portion "**comprises**" at least 30 or 50 contiguous amino acid residues of the polypeptide encoded by the cDNA contained in ATCC Deposit Number 75875 or 75873 that specifically binds to protein such as the ones recited in claims 65-74, (14) the antibody or fragment thereof that specifically binds to *any* protein consisting of a portion of the polypeptide encode by the cDNA contained in ATCC Deposit Number 75875 or 75873, wherein said portion "**comprises**" at least 30 or 50 contiguous amino acid residues of the polypeptide encoded by the cDNA contained in ATCC Deposit Number 75875 or 75873 is a human antibody, a polyclonal antibody, a monoclonal antibody, a chimeric antibody, a humanized antibody, a single chain antibody, and an Fab fragment, (15) *any* isolated antibody or fragment thereof mentioned above which is labeled, (16) *any* antibody or fragment thereof mentioned above which is labeled wherein the label is an enzyme, (17) *any* antibody or fragment thereof mentioned above wherein said antibody or fragment specifically binds to said protein in an ELISA, (18) *any* isolated cell or hybridoma that produces "**fragment thereof**" of antibody that specifically binds to any protein consisting of a portion of the polypeptide encode by the cDNA contained in ATCC Deposit Number 75875 or 75873, wherein said portion "**comprises**" at least 30 or 50 contiguous amino acid residues of the polypeptide encoded by the cDNA contained in ATCC Deposit Number 75875 or 75873, and (19) an isolated antibody or fragment thereof obtained from an animal that has been immunized with *any* protein mentioned above for sandwich assays (page 17) or detection assays (page 18).

The specification discloses only two polypeptides of interleukin-1 beta converting enzyme like apoptosis protease 3 (ICE-LAP3) of SEQ ID NO: 2 and ICE-LAP4 of SEQ ID NO: 4 encoded by cDNAs contained in ATCC Deposit Number 75875, and 75873, respectively. The specification further discloses antibodies such as polyclonal, monoclonal, chimeric, single chain, and humanized antibodies as well as antibody fragment thereof such as Fab fragments that binds specifically to polypeptides of interleukin-1 beta converting enzyme like apoptosis protease 3

(ICE-LAP3) of SEQ ID NO: 2 and ICE-LAP4 of SEQ ID NO: 4 encoded by cDNAs contained in ATCC Deposit Number 75875, and 75873, respectively for detection assays such as sandwich assays (page 17) or detection assays (page 18).

With the exception of the specific antibody that binds to the specific proteins mentioned above, there is inadequate written description about the structure associated with functions of any isolated antibody or fragment thereof that binds to *any* protein consisting of any portion of SEQ ID NO: 2, SEQ ID NO: 4 or the polypeptides encoded by the deposited cDNA wherein said portion "comprises" at least any 30 or 50 contiguous amino acid residues of SEQ ID NO: 2, SEQ ID NO: 4 or the polypeptides encoded by the deposited cDNA because the term "comprising" is open-ended. It expands the portion to include additional amino acids at either or both end of said portion. There is insufficient written about the undisclosed amino acids to be added. There is insufficient written description about the binding specificity of the claimed antibody or fragment thereof obtained from an animal that has been immunized with *any* protein consisting of any portion of SEQ ID NO: 2 or 4 wherein said portion "comprises" at least any 30 or 50 contiguous amino acid residues of SEQ ID NO: 2 or 4 because of the following reasons. Even if the antibody binds to a portion of SEQ ID NO: 2, SEQ ID NO: 4 wherein the portion consisting of 30 or 50 contiguous amino acid residues of said SEQ ID NO: 2 or SEQ ID NO: 4, there is insufficient written description as to which portion such as which 30 or 50 amino acids of SEQ ID NO: 2 or 4 to be used for generating any antibody that would bind specifically to SEQ ID NO: 2 or 4. There is inadequate written description about the specific amino acid residues that makes up the antigenic determinant for which the antibody binds. Given the indefinite number of undisclosed amino acids that can be added, there is inadequate written description about the undisclosed additional amino acids, let alone which undisclosed antibody would bind to specifically to a protein as set forth in claims 31, 53, 64, and 87. Since the structure of the protein is not disclosed, the antibody binding specificity to said undisclosed protein is not adequately described. Since the antibody binding specificity is not adequately described, it follows that any polyclonal, monoclonal, chimeric, humanized, single chain antibody and Fab fragment are not adequately described.

As to claim 53 (c), (d), (g) (h), 87 (c), (d), (g) (h), although the claim has been amended, it is not clear if the claimed antibody or fragment thereof obtained from an animal that has been immunized with a protein comprising an amino acid sequence of SEQ ID NO: 2, SEQ ID NO: 4, the polypeptide encoded by the cDNA contained in the ATCC Deposit Number 75875 or 75873,

or a protein consisting of at least 30 or 50 contiguous amino acid residues of SEQ ID NO: 2, SEQ ID NO: 4, the polypeptide encoded by the cDNA contained in the ATCC Deposit Number 75875 or 75873 as written. Given the ambiguity of the protein used to immunize the animal, any antibody obtained from any animal using any undisclosed protein is not adequately described.

As to claims 42-48, 62-63, and 75-81, since the binding specificity of the antibody mentioned above is not adequately described, it follows that any monoclonal antibody, any chimeric antibody, any polyclonal antibody and humanized antibody and labeled antibody obtained from *any* animal that has been immunized with said undisclosed protein mentioned above are not adequately described. It also follows that the method of detecting using the undisclosed antibody is not adequately described.

Further, the specification discloses only antibodies that bind two polypeptides of interleukin-1 beta converting enzyme like apoptosis protease 3 (ICE-LAP3) of SEQ ID NO: 2 and ICE-LAP4 of SEQ ID NO: 4 encoded by cDNAs contained in ATCC Deposit Number 75875, and 75873, respectively. Given the lack of a written description of *any* additional representative species of polypeptide to which the antibody binds, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicants' arguments filed 3/7/03 have been fully considered but are not found persuasive.

Applicants' position is that (1) the claimed antibodies bind to sequences disclosed in SEQ ID NO: 2, SEQ ID NO: 4, or encoded by the cDNAs of ATCC Deposited Number 75875 or 75873.

However, claims 31 (c), (d), (g) (h), 64 (c), (d), (g) (h) still recite a protein consisting a portion of ...wherein the portion "comprises" at least 30 or 50 contiguous amino acid residues.... The term "comprising" is open-ended. It expands the portion to include additional amino acids at either or both end of said portion. There is insufficient written about the undisclosed amino acids to be added to which the claimed antibody binds. There is insufficient written description about the binding specificity of the claimed antibody or fragment thereof obtained from an animal that

has been immunized with *any* protein consisting of any portion of SEQ ID NO: 2 or 4 wherein said portion "comprises" at least any 30 or 50 contiguous amino acid residues of SEQ ID NO: 2 or 4. As to claim 53 (c), (d), (g) (h), 87 (c), (d), (g) (h), although the claim has been amended, it is not clear if the claimed antibody or fragment thereof obtained from an animal that has been immunized with a protein comprising an amino acid sequence of SEQ ID NO: 2, SEQ ID NO: 4, the polypeptide encoded by the cDNA contained in the ATCC Deposit Number 75875 or 75873, or a protein consisting of at least 30 or 50 contiguous amino acid residues of SEQ ID NO: 2, SEQ ID NO: 4, the polypeptide encoded by the cDNA contained in the ATCC Deposit Number 75875 or 75873 as written. Given the ambiguity of the protein used to immunize the animal, any antibody obtained from any animal using any undisclosed protein is not adequately described. With regard to any isolated cell or hybridoma (claims 49-50, and 82-83) that produce "antibody fragment thereof", there is insufficient written about the hybridoma that produce which antibody fragment, let alone which coding sequences the cell or hybridoma is engineered with to produce the antibody fragment that specifically binds to protein as set forth in claims 31 and 64.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

10. Claims 46 and 79 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 46 and 79 are improper because dependent claim should be narrower in scope than the claim from which it depends.

Applicants' arguments filed 3/7/03 have been fully considered but are not found persuasive.

Applicants' position is that (1) claims 46 and 79 recite the antibodies of claims 31 and 64 are labeled. Because not all of the antibodies of either claim 31 or claim 64 are labeled.

It is suggested that the claims be recited A labeled antibody or fragment thereof of claims 61 or 64 wherein the antibody is labeled.

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(e) the invention was described in a **patent** granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an **international application** by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

12. The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

13. Claims 31, 34-35, 38-39, 43-44 and 48-50 are rejected under 35 U.S.C. 102(e) as being anticipated by US Pat 5,552,536 (Sept 1996; PTO 1449).

The '536 patent teaches various polyclonal and monoclonal antibodies as well as antibody fragment such as Fab to a polypeptide such as a fragment of ICE related cysteine proteinase III, which is a functional derivatives of the claimed polypeptides of SEQ ID NO: 2 and 4 shown in Figures 1 and 2, respectively, having a pentapeptide sequence Gln-Ala-Cys-Arg-Gly surrounding the catalytic cysteine of ICE or its equivalent CED-3 (See column 1, lines 56-59, column 7, lines 52-59, column 4, lines 65 bridging column 5, lines 1-63, in particular). The reference monoclonal antibody is produced by hybridoma or cell line (See column 5, lines 49, in particular). The term "comprising" is open ended. It expands the claimed polypeptide fragment to include additional amino acid residues at either or both ends to read on the reference polypeptide. Thus, the reference teachings anticipate the claimed invention.

Applicants' arguments filed 3/7/03 have been fully considered but are not found persuasive.

Applicants' position is that (1) claim 22 has been canceled. (2) The subject claims require that the antibodies specifically bind to the recited ICE-LAP-3 or ICE-LAP-4. Even if an antibody can be made which binds to the QACRG consensus sequence alone, such as an antibody would not fall within the subject claims because it would not be specific for ICE-LAP-3 or ICE-LAP-4 polypeptides.

However, the claimed antibody binds to a protein that has stretch of amino acid sequence such as Gln-Ala-Cys-Arg-Gly surrounding the catalytic cysteine of ICE identical to the reference protein. In the absence of a side-by-side comparison, the claimed antibody also binds to the reference protein and the reference antibody also binds to the claimed protein. Since the Patent Office does not have the facilities for examining and comparing the antibodies of the instant invention to those of the prior art, the burden is on applicant to show that the prior art antibody is different from the claimed antibody. See In re Best, 562 F.2d 1252, 195 USPQ 430(CCPA 1977).

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 31, 34-35, 38-39, 43-44 and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cerretti *et al* (Science 256: 97-100, April 1992; PTO 892) in view of Campbell *et al* (in Monoclonal Antibody Technology, 1984, Elsevier Science Publisher, New York, NY, page 1-32; PTO 892).

Cerretti *et al* teach human interleukin-1β converting enzyme that has a region such as QACRG within the reference polypeptide that is 100% identical to the claimed polypeptide fragments having the deduced amino acid sequence of polypeptide of SEQ ID NO: 3 as shown in Figure 1 and polypeptide of SEQ ID NO: 4 as shown in Fig 2 (See page 98, Fig 1, Cys 285, in particular). Cerretti *et al* teach molecular cloning of human interleukin-1β converting enzyme offers new target for the development of therapeutic agents for suppressing host immune and

inflammatory response (See abstract, page 99, column 2, last paragraph, in particular). The term "comprising" is open ended. It expands the claimed polypeptide fragment to include additional amino acid residues at either or both ends.

The claimed invention as recited in claim 31 differs from the reference only that an isolated antibody or fragment thereof that specifically binds to a protein consisting of a portion of SEQ ID NO: 2 wherein said portion comprises at least 30 contiguous amino acid residues of SEQ ID NO: 2 and a protein a protein consisting of a portion of SEQ ID NO: 2 wherein said portion comprises at least 50 contiguous amino acid residues of SEQ ID NO: 2, a protein consisting of a portion of SEQ ID NO: 4 wherein said portion comprises at least 30 contiguous amino acid residues of SEQ ID NO: 4 and a protein a protein consisting of a portion of SEQ ID NO: 4 wherein said portion comprises at least 50 contiguous amino acid residues of SEQ ID NO: 4.

The claimed invention as recited in claim 34 differs from the reference only that the antibody or fragment thereof specifically binds to a protein consisting of a portion of SEQ ID NO: 2 wherein said portion comprises at least 30 contiguous amino acid residues of SEQ ID NO: 2.

The claimed invention as recited in claim 35 differs from the reference only that the antibody or fragment thereof specifically binds to a protein consisting of a portion of SEQ ID NO: 2 wherein said portion comprises at least 50 contiguous amino acid residues of SEQ ID NO: 2.

The claimed invention as recited in claim 38 differs from the reference only that the antibody or fragment thereof specifically binds to a protein consisting of a portion of SEQ ID NO: 4 wherein said portion comprises at least 30 contiguous amino acid residues of SEQ ID NO: 4.

The claimed invention as recited in claim 39 differs from the reference only that the antibody or fragment thereof specifically binds to a protein consisting of a portion of SEQ ID NO: 4 wherein said portion comprises at least 50 contiguous amino acid residues of SEQ ID NO: 4.

The claimed invention as recited in claim 43 differs from the reference only that the antibody or fragment thereof is a polyclonal antibody.

The claimed invention as recited in claim 44 differs from the reference only that the antibody or fragment thereof is a monoclonal antibody.

The claimed invention as recited in claim 48 differs from the reference only that the antibody or fragment thereof wherein said antibody or fragment thereof specifically binds to said protein in an ELISA.

Campbell *et al* teach that "it is customary now for any group working on a macromolecule to both clone the gene encoding for it and make monoclonal antibodies to it (sometimes without a clear objective for their application)" (See page 29, section Basic Research, in particular). Campbell *et al* further teach conventional antiserum which is polyclonal antibody (See page 4, comparison of monoclonal antibodies and conventional antiserum, in particular).

Therefore, it would be been obvious to one having ordinary skill in the art at the time the invention was made to produce polyclonal or monoclonal antibody that is specific for human interleukin-1β converting enzyme related protease as taught by Cerretti *et al*. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art at the time the invention was made would have been motivated with a reasonable expectation of success to generate polyclonal or monoclonal antibodies to the claimed polypeptide based on the fact that it is a conventional practice in the art to do so for further study, characterization and identification of a polypeptide as taught by Campbell *et al* since the antibody to the polypeptide of other members of the same family that induces cell death (apoptosis) as taught by Cerretti *et al*. The term "comprising" is open-ended. It expands the polypeptide to which the antibody binds to include additional amino acid residues at either or both ends to read on the reference polypeptide as taught by Cerretti *et al*. Claim 48 is included in this rejection because the binding specificity of the reference antibody to the protein is the same irrespective of where the protein is located such as on a gel, or in ELISA plate.

Applicants' arguments filed 3/7/03 have been fully considered but are not found persuasive.

Applicants' position is that (1) claim 22 has been canceled. (2) The subject claims require that the antibodies specifically bind to the recited ICE-LAP-3 or ICE-LAP-4. Even if an antibody can be made which binds to the QACRG consensus sequence alone, such as an antibody would not fall within the subject claims because it would not be specific for ICE-LAP-3 or ICE-LAP-4 polypeptides.

However, the claimed antibody binds to a protein that has stretch of amino acid sequence such as Gln-Ala-Cys-Arg-Gly surrounding the catalytic cysteine of ICE identical to the reference

protein. In the absence of a side-by-side comparison, the claimed antibody also binds to the reference protein and the reference antibody also binds to the claimed protein. Since the Patent Office does not have the facilities for examining and comparing the antibodies of the instant invention to those of the prior art, the burden is on applicant to show that the prior art antibody is different from the claimed antibody. See In re Best, 562 F.2d 1252, 195 USPQ 430(CCPA 1977).

17. Claims 31 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cerretti *et al* (Science 256: 97-100, April 1992; PTO 892) or US Pat 5,552,536 (Sept 1996; PTO 1449) each in view of US Pat No. 5,530,101, filed Dec 1990; PTO 892).

The teachings of Cerretti *et al* and the '536 patent have been discussed supra.

The claimed invention in claim 45 differs from the references only by the recitation of said antibody is chimeric, or humanized.

The '101 patent teaches a method of producing chimeric antibodies (See column 11 lines 53-65, in particular) and humanized antibodies (See column 19 line 27-30; column 38, line 54, in particular). The '101 patent further teaches that humanized immunoglobulins (antibodies) will be substantially non-immunogenic in humans and retain substantially the same affinity as the donor immunoglobulin to the antigen (See column 3, lines 32-37, in particular) and will be particularly useful in treating human disorders susceptible to monoclonal antibody therapy (See column 2, line 54-56, in particular).

Therefore, it would be been obvious to one having ordinary skill in the art at the time the invention was made to produce humanized or chimeric antibody that is specific for the reference human interleukin-1β converting enzyme related protease as taught by Cerretti *et al* and the '536 patent. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art at the time the invention was made would have been motivated with an expectation of success to produce chimeric or humanized antibodies because the '101 patent further teaches that humanized immunoglobulins (antibodies) will be substantially non-immunogenic in humans and retain substantially the same affinity as the donor immunoglobulin to the antigen (See column 3, lines 32-37, in particular) and will be particularly useful in treating human disorders susceptible to monoclonal antibody therapy (See column 2, line 54-56, in particular). Cerretti *et al* teach molecular cloning of human interleukin-1β converting enzyme offers new target for the development of therapeutic agents for suppressing

host immune and inflammatory response (See abstract, page 99, column 2, last paragraph, in particular).

Applicants' arguments filed 3/7/03 have been fully considered but are not found persuasive.

Applicants' position is that (1) claim 22 has been canceled. (2) The subject claims require that the antibodies specifically bind to the recited ICE-LAP-3 or ICE-LAP-4. Even if an antibody can be made which binds to the QACRG consensus sequence alone, such as an antibody would not fall within the subject claims because it would not be specific for ICE-LAP-3 or ICE-LAP-4 polypeptides.

However, the claimed antibody binds to a protein that has stretch of amino acid sequence such as Gln-Ala-Cys-Arg-Gly surrounding the catalytic cysteine of ICE identical to the reference protein. In the absence of a side-by-side comparison, the claimed antibody also binds to the reference protein and the reference antibody also binds to the claimed protein. Since the Patent Office does not have the facilities for examining and comparing the antibodies of the instant invention to those of the prior art, the burden is on applicant to show that the prior art antibody is different from the claimed antibody. See In re Best, 562 F.2d 1252, 195 USPQ 430(CCPA 1977).

18. Claims 31, 43-44 and 49-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cerretti *et al* (Science 256: 97-100, April 1992; PTO 892) in view of Harlow *et al* (in Antibodies a Laboratory Manual, 1988, Cold Spring harbor laboratory publication, Cold Spring Harbor, NY, pages 92-94, pages 116-117, pages 626-629).

The teachings of Cerretti *et al* have been discussed supra.

The claimed invention in claim 43 differs from the reference only by the recitation that the antibody is polyclonal antibody.

The claimed invention in claim 44 differs from the reference only by the recitation that the antibody is monoclonal antibody.

The claimed invention in claim 49 differs from the reference only by the recitation that an isolated cell that produces the antibody that binds to a protein consisting of a portion of SEQ ID NO: 4 wherein said portion comprises at least 30 contiguous amino acid residues of SEQ ID NO: 4 and a protein a protein consisting of a portion of SEQ ID NO: 4 wherein said portion comprises at least 50 contiguous amino acid residues of SEQ ID NO: 4.

The claimed invention in claim 50 differs from the reference only by the recitation that a hybridoma that produces the antibody or fragment thereof that binds to a protein consisting of a portion of SEQ ID NO: 4 wherein said portion comprises at least 30 contiguous amino acid residues of SEQ ID NO: 4 and a protein a protein consisting of a portion of SEQ ID NO: 4 wherein said portion comprises at least 50 contiguous amino acid residues of SEQ ID NO: 4.

Harlow *et al* teach a method of producing polyclonal or monoclonal antibody that is produced by a hybridoma or cell line (See page 92-94, page 116-117 in particular). Harlow *et al* teach a method of producing polyclonal antibody to any antigen (See page 93, in particular). Harlow *et al* further teach that for practical reasons, rabbits represent a good choice for the routine production of polyclonal sera since they are easy to keep and handle and antibody produced are well characterized and easily purified.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to produce polyclonal or monoclonal antibody and antibody fragment as taught by Harlow *et al* with the human interleukin-1β converting enzyme related protease that has a pentapeptide that is conserved in all members of the ICE protease family as taught by Cerretti *et al*. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to make monoclonal and polyclonal antibody fragment because Harlow *et al* teach that antibody fragments such as Fab can overcome the problem of capping and internalization of the antigen on mammalian cell when using multivalent antibodies (See page 626 in particular). Cerretti *et al* teach molecular cloning of human interleukin-1β converting enzyme offers new target for the development of therapeutic agents for suppressing host immune and inflammatory response (See abstract, page 99, column 2, last paragraph, in particular).

Applicants' arguments filed 3/7/03 have been fully considered but are not found persuasive.

Applicants' position is that (1) claim 22 has been canceled. (2) The subject claims require that the antibodies specifically bind to the recited ICE-LAP-3 or ICE-LAP-4. Even if an antibody can be made which binds to the QACRG consensus sequence alone, such as an antibody would not fall within the subject claims because it would not be specific for ICE-LAP-3 or ICE-LAP-4 polypeptides.

However, the claimed antibody binds to a protein that has stretch of amino acid sequence such as Gln-Ala-Cys-Arg-Gly surrounding the catalytic cysteine of ICE identical to the reference protein. In the absence of a side-by-side comparison, the claimed antibody also binds to the reference protein and the reference antibody also binds to the claimed protein. Since the Patent Office does not have the facilities for examining and comparing the antibodies of the instant invention to those of the prior art, the burden is on applicant to show that the prior art antibody is different from the claimed antibody. See In re Best, 562 F.2d 1252, 195 USPQ 430(CCPA 1977).

19. Claims 31 and 45-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cerretti *et al* (Science 256: 97-100, April 1992; PTO 892) in view of Harlow *et al* (in Antibodies a Laboratory Manual, 1988, Cold Spring harbor laboratory publication, Cold Spring Harbor, NY, pages 319-356, and 626-629).

The teachings of Cerretti *et al* have been discussed supra.

The claimed invention as recited in claim 45 differs from the reference only by the recitation that the antibody is a Fab fragment.

The claimed invention as recited in claim 46 differs from the reference only by the recitation that the antibody is labeled.

The claimed invention as recited in claim 47 differs from the reference only by the recitation that the labeled antibody wherein the label is an enzyme.

Harlow *et al* teach a method of producing antibody fragment wherein the fragment is Fab fragment (See page 626-629, in particular). Harlow *et al* teach that the problems of using multivalent antibodies on mammalian cells often will lead to capping and internalization of the antigen which can be overcome by using fragments of antibodies (See page 626 in particular). Harlow *et al* further teach labeling any antibody with various labels such as enzyme (See chapter 9, in particular) for various detection assays. The advantages of enzyme labeling are longer shelf life, and higher sensitivity (See page 322, in particular).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to produce antibody fragment such as Fab or to label any antibody as taught by Harlow *et al* with the polyclonal antibody that binds specific to the polypeptide fragment as taught by Cerretti *et al*. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because Harlow *et al* teach antibody fragments can overcome the problem of capping and internalization of the antigen on mammalian cell when using multivalent antibodies (See page 626 in particular) and the labeled antibody can be used for various detection assays. The advantages of enzyme labeling are longer shelf life, higher sensitivity while the advantages of fluorochrome label are long shelf life and good resolution in immunohistochemistry (See page 322, in particular).

Applicants' arguments filed 3/7/03 have been fully considered but are not found persuasive.

Applicants' position is that (1) claim 22 has been canceled. (2) The subject claims require that the antibodies specifically bind to the recited ICE-LAP-3 or ICE-LAP-4. Even if an antibody can be made which binds to the QACRG consensus sequence alone, such as an antibody would not fall within the subject claims because it would not be specific for ICE-LAP-3 or ICE-LAP-4 polypeptides.

However, the claimed antibody binds to a protein that has stretch of amino acid sequence such as Gln-Ala-Cys-Arg-Gly surrounding the catalytic cysteine of ICE identical to the reference protein. In the absence of a side-by-side comparison, the claimed antibody also binds to the reference protein and the reference antibody also binds to the claimed protein. Since the Patent Office does not have the facilities for examining and comparing the antibodies of the instant invention to those of the prior art, the burden is on applicant to show that the prior art antibody is different from the claimed antibody. See In re Best, 562 F.2d 1252, 195 USPQ 430(CCPA 1977).

20. Claims 31 and 46-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat 5,552,536 (Sept 1996; PTO 1449) in view of Harlow *et al* (in Antibodies a Laboratory Manual, 1988, Cold Spring harbor laboratory publication, Cold Spring Harbor, NY, pages 319-356, and 626-629).

The teachings of the '536 patent have been discussed supra.

The claimed invention as recited in claim 46 differs from the reference only by the recitation that the antibody is labeled.

The claimed invention as recited in claim 47 differs from the reference only by the recitation that the labeled antibody wherein the label is an enzyme.

Harlow *et al* teach labeling any antibody with various labels such as enzyme (See chapter 9, in particular) for various detection assays. The advantages of antibody labeling with an enzyme are longer shelf life, and higher sensitivity (See page 322, in particular).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to label any antibody with an enzyme as taught by Harlow *et al* with the polyclonal or monoclonal antibody that binds specific to the polypeptide fragment as taught by the '536 patent. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because Harlow *et al* teach the advantages of enzyme labeling are longer shelf life, higher sensitivity while the advantages of fluorochrome label are long shelf life and good resolution in immunohistochemistry (See page 322, in particular).

Applicants' arguments filed 3/7/03 have been fully considered but are not found persuasive.

Applicants' position is that (1) claim 22 has been canceled. (2) The subject claims require that the antibodies specifically bind to the recited ICE-LAP-3 or ICE-LAP-4. Even if an antibody can be made which binds to the QACRG consensus sequence alone, such as an antibody would not fall within the subject claims because it would not be specific for ICE-LAP-3 or ICE-LAP-4 polypeptides.

However, the claimed antibody binds to a protein that has stretch of amino acid sequence such as Gln-Ala-Cys-Arg-Gly surrounding the catalytic cysteine of ICE identical to the reference protein. In the absence of a side-by-side comparison, the claimed antibody also binds to the reference protein and the reference antibody also binds to the claimed protein. Since the Patent Office does not have the facilities for examining and comparing the antibodies of the instant invention to those of the prior art, the burden is on applicant to show that the prior art antibody is different from the claimed antibody. See In re Best, 562 F.2d 1252, 195 USPQ 430(CCPA 1977).

21. Claims 31 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cerretti *et al* (Science 256: 97-100, April 1992; PTO 892) or US Pat 5,552,536 (Sept 1996; PTO 1449) each in view of US Pat No. 5,260,203 (Nov 1993, PTO 892).

The teachings of Cerretti *et al* and the '536 patent have been discussed supra.

The claimed invention in claim 45 differs from the references only by the recitation that the antibody is a single chain antibody.

The '203 patent teaches a method of producing single chain antibody comprising a variable region of any antibody or a polypeptide fragment (See column 29, lines 25 bridging column 30, lines 1-20, in particular). The advantages of a single chain antibody are small size, greater stability, significantly reduced cost and could be engineered to be highly antigenic and yet reduce the body's immunologic reaction and thus increase the safety and efficacy of the therapeutic application (See column 3, lines 33-48, in particular).

Therefore, it would be been obvious to one having ordinary skill in the art at the time the invention was made to make single chain antibody as taught by the '203 patent that binds specifically to the polypeptide and fragment thereof as taught by the Cerretti *et al* or the '536 patent for detection assays as taught by the '536 patent. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art at the time the invention was made would have been motivated to do this because the '203 patent teaches the advantages of a single chain antibody are small size, greater stability, significantly reduced cost and could be engineered to be highly antigenic and yet reduce the body's immunologic reaction and thus increase the safety and efficacy of the therapeutic application (See column 3, lines 33-48, in particular).

Applicants' arguments filed 3/7/03 have been fully considered but are not found persuasive.

Applicants' position is that (1) claim 22 has been canceled. (2) The subject claims require that the antibodies specifically bind to the recited ICE-LAP-3 or ICE-LAP-4. Even if an antibody can be made which binds to the QACRG consensus sequence alone, such as an antibody would not fall within the subject claims because it would not be specific for ICE-LAP-3 or ICE-LAP-4 polypeptides.

However, the claimed antibody binds to a protein that has stretch of amino acid sequence such as Gln-Ala-Cys-Arg-Gly surrounding the catalytic cysteine of ICE identical to the reference protein. In the absence of a side-by-side comparison, the claimed antibody also binds to the reference protein and the reference antibody also binds to the claimed protein. Since the Patent Office does not have the facilities for examining and comparing the antibodies of the instant

invention to those of the prior art, the burden is on applicant to show that the prior art antibody is different from the claimed antibody. See In re Best, 562 F.2d 1252, 195 USPQ 430(CCPA 1977).

22. The following new ground of rejection is necessitated by the amendment filed 3/7/03.

23. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

24. Claims 53, 64, and 87 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949).

The recitation of "a protein comprising an amino acid sequence of SEQ ID NO: 2 consisting of at least 30 contiguous amino acid residues of SEQ ID NO: 2" in claims 53 (c)

In the present instance, claim 53 (c) recites the broad recitation a protein comprising an amino acid sequence of SEQ ID NO: 2, and the claim also recites a protein consisting of at least 30 contiguous amino acid resides of SEQ OID NO: 2 which is the narrower statement of the range/limitation.

Claim 53 (d) recites the broad recitation a protein comprising an amino acid sequence of SEQ ID NO: 2, and the claim also recites a protein consisting of at least 50 contiguous amino acid resides of SEQ OID NO: 2 which is the narrower statement of the range/limitation.

Claim 53 (g) recites the broad recitation a protein comprising an amino acid sequence of SEQ ID NO: 4, and the claim also recites a protein consisting of at least 30 contiguous amino acid resides of SEQ OID NO: 4 which is the narrower statement of the range/limitation.

Claim 53 (4) recites the broad recitation a protein comprising an amino acid sequence of SEQ ID NO: 4, and the claim also recites a protein consisting of at least 50 contiguous amino acid resides of SEQ OID NO: 4 which is the narrower statement of the range/limitation.

Claim 64(c) recites the broad recitation a portion comprises at least 30 contiguous amino acid residues of polypeptide encoded by the cDNA contained in ATCC Deposit Number 75875 and the claim also recites a protein consisting of a portion of the polypeptide encoded by the cDNA contained in ATCC Deposit Number 75875 which is the narrower statement of the range/limitation.

Claim 64(d) recites the broad recitation a portion comprises at least 50 contiguous amino acid residues of polypeptide encoded by the cDNA contained in ATCC Deposit Number 75875 and the claim also recites a protein consisting of a portion of the polypeptide encoded by the cDNA contained in ATCC Deposit Number 75875 which is the narrower statement of the range/limitation.

Claim 64(g) recites the broad recitation a portion comprises at least 30 contiguous amino acid residues of polypeptide encoded by the cDNA contained in ATCC Deposit Number 75873 and the claim also recites a protein consisting of a portion of the polypeptide encoded by the cDNA contained in ATCC Deposit Number 75873 which is the narrower statement of the range/limitation.

Claim 64(h) recites the broad recitation a portion comprises at least 50 contiguous amino acid residues of polypeptide encoded by the cDNA contained in ATCC Deposit Number 75873 and the claim also recites a protein consisting of a portion of the polypeptide encoded by the cDNA contained in ATCC Deposit Number 75873 which is the narrower statement of the range/limitation.

Claim 87(c) recites the broad recitation a portion comprising an amino acid sequence of the polypeptide encoded by the cDNA contained in ATCC Deposit Number 75875 and the claim also recites a protein consisting of at least 30 contiguous amino acid residues of polypeptide encoded by the cDNA contained in ATCC Deposit Number 75875 which is the narrower statement of the range/limitation.

Claim 87(d) recites the broad recitation a portion comprising an amino acid sequence of the polypeptide encoded by the cDNA contained in ATCC Deposit Number 75875 and the claim also recites a protein consisting of at least 50 contiguous amino acid residues of polypeptide encoded by the cDNA contained in ATCC Deposit Number 75875 which is the narrower statement of the range/limitation.

Claim 87(g) recites the broad recitation a portion comprising an amino acid sequence of the polypeptide encoded by the cDNA contained in ATCC Deposit Number 75873 and the claim also recites a protein consisting of at least 30 contiguous amino acid residues of polypeptide encoded by the cDNA contained in ATCC Deposit Number 75873 which is the narrower statement of the range/limitation.

Claim 87(h) recites the broad recitation a portion comprising an amino acid sequence of the polypeptide encoded by the cDNA contained in ATCC Deposit Number 75873 and the claim also recites a protein consisting of at least 50 contiguous amino acid residues of polypeptide encoded by the cDNA contained in ATCC Deposit Number 75873 which is the narrower statement of the range/limitation.

25. Claims 98-107 stand allowed.

26. Claims 32, 33, 36-37, 54 and 58 stand objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

27. No claim is allowed.

28. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

29. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

30. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Phuong N. Huynh, Ph.D.
Patent Examiner
Technology Center 1600
June 2, 2003

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